FORM PTO-1390 (Modified) (REV 11-2000) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 0702-1216

U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR 1 5): 10/088582

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/DK99/00522	4 October 1999	

TITLE OF INVENTION
Sensor for Measuring Tissue Perfusion

APPLICANT(S) FOR DO/EO/US
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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S C. 371 (c) (2))
   a. ☒ is attached hereto (required only if not communicated by the International Bureau).
   b. ☐ has been communicated by the International Bureau
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U S.C 371(c)(2)).
   a ☒ is attached hereto
   b. ☐ has been previously submitted under 35 U.S C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C 371 (c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b ☒ have been communicated by the International Bureau.
   c ☐ have not been made; however, the time limit for making such amendments has NOT expired
   d ☐ have not been made and will not be made
8. ☒ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S C 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U S C 371 (c)(4)).
10. ☒ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5))
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☒ An Information Disclosure Statement under 37 CFR 1 97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3 31 is included.
15. ☐ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter 2 and 35 U.S.C. 1.821 - 1.825
20. ☐ A second copy of the published international application under 35 U S.C. 154(d)(4)
21. ☐ A second copy of the English language translation of the international application under 35 U S C. 154(d)(4)
22. ☒ Certificate of Mailing by Express Mail
23. ☐ Other items or information:

JC10 Rec'd PCT/PTO 20 MAR 2002

U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/088582	PCT/DK99/00522	0702-1216

24. The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
☐ Neither international preliminary examination fee (37 CFR 1 482) nor international search fee (37 CFR 1 445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**		
☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**		
☐ International preliminary examination fee (37 CFR 1 482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**		
☐ International preliminary examination fee (37 CFR 1 482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) . . **$710.00**		
☐ International preliminary examination fee (37 CFR 1 482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	**$890.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492 (e))	**$130.00**	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	16 - 20 =	0	x $18.00	**$0.00**	
Independent claims	1 - 3 =	0	x $84 00	**$0.00**	
Multiple Dependent Claims **(check if applicable)**			☒	**$280.00**	
TOTAL OF ABOVE CALCULATIONS =				**$1,300.00**	
☒ Applicant claims small entity status See 37 CFR 1.27) The fees indicated above are reduced by 1/2.				**$650.00**	
SUBTOTAL =				**$650.00**	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)) +				**$0.00**	
TOTAL NATIONAL FEE =				**$650.00**	
Fee for recording the enclosed assignment (37 CFR 1 21(h)) The assignment must be accompanied by an appropriate cover sheet (37 CFR 3 28, 3 31) **(check if applicable).** ☐				**$0.00**	
TOTAL FEES ENCLOSED =				**$650.00**	
				Amount to be: refunded	$
				charged	$

a. ☒ A check in the amount of **$650.00** to cover the above fees is enclosed

b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No **12-0913** A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO

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34,128
REGISTRATION NUMBER

3-20-2002
DATE

SENSOR FOR MEASURING TISSUE PERFUSION

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to devices for measurements of tissue perfusion according to the preamble of independent claim 1 and more particularly to a sensor for measurement of tissue perfusion over a given variable region and having a short response time.

BACKGROUND ART

Tissue perfusion is a measure of the amount (volume) of blood passing through a unit quantity of the tissue and is often measured with the unit ml blood/100 g tissue. Since all blood tissues are at the same time being supplied with nutrients and excrete waste products through diffusion between tissue cells and the blood, tissue perfusion is a very important factor indicating the state of health of a tissue. A method for the measurement of tissue perfusion is therefore highly pertinent, for instance for monitoring tissue during and after surgical operations and transplantations. Monitoring of potentially threatened tissue, e.g. muscular tissue, whose blood supply may become adversely affected by increasing pressure in the connective tissue membrane of the muscle, would be highly pertinent as an indication of when a pressure relieving operation should be initiated. Likewise monitoring of internal perfusion caused by the formation of oedemas in a heart stopped during operation could provide valuable information about the need of external supply of nutrients to the tissue of the heart. Within medical research, perfusion is an important parameter too.

A number of methods for determination of tissue perfusion are known. A technique consisting of an injection into the relevant tissue of radioactive xenon as a tracer and measuring the decay of radioactivity as a function of time has been described (see Larsen et al., 1966. Blood Flow through Human Adipose Tissue Determined

with Radioactive Xenon. Acta physiol. scand. 66, pp 337-345), but this technique suffers from a number of drawbacks in that its temporal resolution only amounts to approximately half an hour which is insufficient in many situations. Furthermore the location of the injection of the radioactive matter into the tissue relative to the location where the radioactivity is being measured is not particularly well-defined and finally, the application of radioactive matter per se involves potential hazards.

Another method of measuring tissue perfusion utilises continuous injection of ethanol during microdialysis. During microdialysis a fluid is being pumped very slowly through a fibre inserted into the tissue of the patient. The concentration of the fluid is in equilibrium with the surrounding tissue as the catheter is diffusion-open and the fluid is being collected via a return fibre. This method also suffers from an insufficient temporal resolution.

WO 97/46853 discloses a method and a microsensor which is able to measure tissue perfusion. The sensor comprises a tracer-permeable insert placed in a mouth of a tracer reservoir confined by a container, whereby said insert forms a permeable wall portion of the reservoir. A sensoric tip of a transducer is placed inside the insert or immediately outside of the latter. From the specification as a whole it appears that the tip of the transducer is very small, a diameter of 2 μm being mentioned. Consequently the transducer detects or measures the tracer concentration or pressure in a single point or in an extremely limited area. This also applies, if the transducer is provided with an inner cylindrical cavity, which is closed by the permeable insert or by a separate membrane forming the end wall of the transducer.

In connection with monitoring tissue perfusion for instance during surgical operations, the above-mentioned prior art suffers from the drawbacks of either insufficient temporal resolution or a very limited measurement space.

DISCLOSURE OF THE INVENTION

In order to circumvent the drawbacks and limitations of methods and devices for the measurement of tissue perfusion of prior art as mentioned above, it is the object of the present invention to provide a device (sensor) for the measurement of tissue perfusion which is able to integrate measurements of tissue perfusion over a larger

region in the tissue, the dimensions of which region can be varied as desired.

It is a further object of the present invention to provide a device with a response time not exceeding a few minutes.

It is a further object of the present invention to provide at least one embodiment of the general inventive idea which makes it possible to carry out non-invasive measurements of skin perfusion or measurements of prefusion in the surface layers of an organ, for instance for assessment of insufficient blood circulation.

These objects are accomplished with a device (sensor) according to the characterising clause of claim 1.

Various advantageous embodiments of the invention are defined in the dependent claims.

In the sensor for tissue perfusion according to the invention a fluid or gaseous tracer from a suitable supply means is supplied to a reservoir in which a constant high concentration of the tracer is maintained through diffusion from the supply means and from which reservoir a small portion of the tracer molecules will diffuse into a tracer-permeable barrier which is partly in contact with the surrounding tissue. From this barrier, part of the tracer molecules will move out into the surrounding tissue via a first spatially extended area, whereas another portion of the tracer molecules will move into an adjoining detector cavity via a second spatially extended area, said detector cavity being in communication with a suitable detector apparatus measuring the concentration of tracer in the detection cavity. The movement of tracer molecules from the reservoir into the surrounding tissue thus takes place via a tracer-permeable barrier which is in contact with the surrounding tissue via said first spatially extended area and the portion of the tracer molecules moving into the detection cavity arrives at the detection cavity via a tracer-permeable barrier and said second spatially extended area. Said first area thus constitutes the area of contact between said tracer-permeable barrier and the surrounding tissue, whose perfusion is to be measured, whereas said second area constitutes the area through which tracer molecules are able to reach the detection cavity. The distribution between the diffusion to the surrounding tissue and the diffusion to the detection cavity will be determined by the flow of dissolve matter in the surrounding tissue, i.e. the

perfusion, such that if the transport in the tissue is of large magnitude only a small portion of the tracer will diffuse into the detection cavity and vice versa. The signal from the detection apparatus will thus become a measure of tissue perfusion in the region surrounding the fibre.

According to the present invention the dimensions of the contact region between said tracer-permeable barrier and the surrounding tissue can be varied and thereby the region over which the tissue perfusion measurement is being carried out. It is also possible to vary the second area providing access to the detection cavity. By varying the geometry of the sensor, i.e. the relative layout of the reservoir, barrier and detection cavity, it is possible to vary the sensitivity and the radial resolution of the measurements being performed. It is furthermore possible to utilise a mixture of at least two tracers which might be supplied and removed substantially momentarily. A time-based measurement after instantaneous supply/removal to/from the tracer reservoir of two tracers with different diffusion coefficients will make it possible to distinguish between how much of the diffusion of the tracers away from the tracer reservoir is due to the concentration gradient within the tissue and how much is due to the transportation of the tracers away from the tissue by the blood. Thus, independent measures of perfusion and of diffusion coefficients within the tissue can be obtained.

It is furthermore possible to carry out measurements of O_2 and CO_2 and other gasses present in the tissue simultaneously with tissue perfusion.

As a suitable tracer for tissue perfusion measurements for instance helium, argon or hydrogen could be used, but it would also be possible to use other tracers.

Finally for in-situ calibration purposes the patient can inhale a gas which is being detected by the sensor placed in the tissue.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be described by way of exemplifying embodiments hereof and with reference to the accompanying drawings in which

Figure 1a is a longitudinal section of a first embodiment of a sensor according to the present invention;

Figure 1b is a cross section along the line indicated by A-A in Figure 1a;

Figure 2a is a longitudinal section of a second embodiment of a sensor according to the present invention;

Figure 2b is a cross section along the line indicated by B-B in Figure 2a;

Figure 3a is a side elevation cross-sectional view of a first version of a fourth embodiment of the present invention;

Figure 3b is a side elevation cross-sectional view of a second version of a fourth embodiment of the present invention;

Figure 4a is a side elevation cross-sectional view of a first version of a fifth embodiment of the present invention comprising interlaced reservoir- and detection cavity sections;

Figure 4b is a side elevation cross-sectional view of a second version of a fifth embodiment of the present invention comprising interlaced reservoir- and detection cavity sections;

Figure 5 is the response of a microsensor according to the invention as a function of time for a sudden change of perfusion obtained in a specific experiment; and

Figure 6 is a calibration curve of the sensor, i.e. the signal from the sensor as a function of the velocity of water obtained in the same experiment as mentioned in connection with Figure 5.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

In the following detailed part of the present description a number of different embodiments of the present invention will be described with reference to the accompanying drawings, but it is understood that these embodiments only constitute examples of the general inventive idea, and that other embodiments may

be conceivable by a person skilled in the art.

The first embodiment of the sensor is shown in Figure 1a and Figure 1b. The sensor is substantially symmetrical about a vertical plane 11 and comprises two U-shaped profiles 1, 2, the reservoir profile 1 and the detection profile 2 made of a gas-impermeable material such as metal or a suitable plastic material. The open sides 12, 13 of these two profiles 1, 2 are both in sealing abutment with a barrier 3 disposed between the reservoir 4 and the detection cavity 5 and extending throughout the vertical length of the sensor. The barrier 3 is made from a gas-permeable material, such as silicon or Teflon, such that two cavities, the reservoir 4 and the detection cavity 5, are defined. At the distal end hereof both the reservoir 4 and the detection cavity 5 are closed by a gas-impermeable barrier 6. At its proximal end the reservoir 4 is provided with an open inlet 7 which via a tube (not shown) is in communication with a supply container (also not shown) containing a gaseous tracer (for instance helium). The outer walls of both the tube and the container are made from a gas-impermeable material. The detection cavity 5 is at its proximal end provided with an open outlet 8 which via a tube (not shown) is in communication with a detector apparatus (vacuum pump and mass spectrometer as it is well-known within the art). The tube between the outlet 8 and the detector apparatus is made from a gas-impermeable and pressure resistant material. The reservoir profile 4, the detection cavity profile 5 and the barriers 3, 6 will in the following be referred to as the fibre.

The fibre is designed to be positioned within the tissue of a patient whose perfusion in that part of the tissue is to be measured. The functional principle of the invention is that a constantly high concentration of the tracer is maintained in the reservoir 4, the concentration being maintained via diffusion from the supply container. A small portion of the molecules of the tracer will due to diffusion move from the reservoir 4 out into the gas-permeable barrier 3 and a portion hereof will move out into the surrounding tissue through a first area 18, as indicated by the arrows 9, while another portion will move into the detection cavity 5 through a second area 13, as indicated by the arrows 10, and eventually be detected by means of the detection apparatus. The distribution between the diffusion to the surrounding tissue and the

diffusion to the detection cavity 5 will be determined by the transport of dissolved matter in the surrounding tissue, such that if the transport in the tissue is of a large magnitude only a small portion of the tracer will diffuse into the detection cavity 5 and vice versa. The signal from the detection apparatus will thus become a measure of tissue perfusion in the region surrounding the fibre.

Figure 2a and Figure 2b show a second embodiment of the present invention. Throughout the following description of the second embodiment of the present invention, elements identical with elements of the first embodiment shown in Figure 1a and Figure 1b will be designated by the same reference numerals as on Figure 1a and Figure 1b. The second embodiment is also substantially symmetrical about a vertical plane 11 and comprises two tubes: the reservoir tube 14 defining the reservoir 4 and the detection tube 15 defining the detection cavity 5, both tubes being made from a semi-gas-impermeable material (plastics). These two tubes 14, 15 are separated from each other by a barrier 19 made from a gas-impermeable material, such as metal or plastics. At the distal end, both the reservoir 4 and the detection cavity 5 are closed by a gas-impermeable barrier 6. At its proximal end the reservoir tube 14 is provided with an open inlet 7 which via a tube with gas-impermeable wall (not shown) is in communication with a supply container constructed from a gas-impermeable material containing a gaseous tracer (for instance helium). The detection tube 5 is at its proximal end provided with an outlet 8 communicating via a pressure resistant tube with gas-impermeable wall with a detection apparatus (vacuum pump and mass spectrometer as it is well-known within the art). The reservoir tube 14, the detection tube 15 and the barriers 6, 19 will in the following be referred to as the fibre.

The fibre is designed to be positioned within the tissue of a patient whose perfusion in that part of the tissue is to be measured. The functional principle of the invention is that a constantly high concentration of the tracer is maintained in the reservoir 4, the concentration being maintained via diffusion from the supply container. A small portion of the molecules of the tracer will due to diffusion move from the reservoir 4 out through the wall of the reservoir tube 14 through a first area 14' (as delimited by the two arrows C in Figure 2b) and into the surrounding tissue, as indicated by the

arrows 9. Of this quantity of tracer, a portion will diffuse into the detection tube and pass through the wall (15) through a second area 15' (as delimited by the two arrows D in Figure 2b) to the detection cavity 5 as indicated by the arrows 16, from where it will be detected by the detection apparatus. The quantity reaching the detection cavity will depend on the transport conditions in the tissue through which diffusion takes place, and the signal from the detector will thus be a measure of the transport conditions, i.e. the perfusion, in the region around the fibre.

A third embodiment (not shown) of the present invention is directly derivable from the two first embodiments described above in that the structures shown in Figure 1 and Figure 2 are helically wound around the longitudinal axis 11 of the fibres. This has the effect of making the sensitivity of the fibres in a plane perpendicular to the longitudinal axis omnidirectional. A suitable pitch of the helix could for instance constitute 10 revolutions per cm.

Figure 3a and 3b show a fourth embodiment of the present invention which differs significantly from the three previous embodiments described above. Where the three above embodiments were designed to be inserted into the tissue, the fourth embodiment of the present invention is fastened non-invasively on the surface (20) of the skin or of an organ of a patient to provide the possibility of carrying out measurements of perfusion in the surface layers of the skin or the organ such as carried out for the assessment of insufficient blood circulation in for instance a leg of the patient.

The operational principle of the first version of the fourth embodiment shown in Figure 3a corresponds to the operational principle of the first embodiment shown in Figure 1a and Figure 1b. The operational principle of the second version of the fourth embodiment shown in Figure 3b corresponds to the operational principle of the second embodiment shown in Figure 2a and Figure 2b.

In the embodiment shown in Figure 3a, the inner side, i.e. the side facing the surface (20) of the skin or organ of the patient, of a gas-impermeable disc 17 is provided with a single one of the sensors according to the first embodiment of the

present invention shown in Figure 1a and Figure 1b. The longitudinal axis 11 of the sensor extends substantially parallel with the plane of said disc 17 and one of the sides 18 of the tracer-permeable barrier 3 is in contact with the surface (20) of the patient's skin or organ. Diffusion of tracer molecules from the barrier 3 into the skin or organ thus only takes place via this single side 18. The function of the disc 17 is to enable sufficient contact pressure between fibre and skin or organ and to prevent escape of tracer molecules in the direction opposite the skin or organ.

In the embodiment shown in Figure 3b the inner side, i.e. the side facing the surface (20) of the skin or organ of the patient, of a gas-impermeable disc 17 is provided with a single one of the sensors according to the second embodiment of the present invention shown in Figure 2a and Figure 2b. The longitudinal axis 11 of the sensor extends substantially parallel with the plane of said disc 17 and parts of the tracer-permeable walls 14 and 15 of the reservoir 4 and detection cavity 5, respectively, are in contact with the surface of the patient's skin or organ. The width w of the tracer-impermeable barrier is modified compared to the second embodiment in order to provide a contact area of sufficient size between the reservoir 4 and the surface of the skin or organ and between the detection cavity 5 and the skin or organ, respectively. Also the side of the reservoir 4 facing away from the detection cavity 5 and the side of the detection cavity 5 facing away from the reservoir 4 are covered with tracer-impermeable barriers 19.

A more preferable variation of the embodiments shown in Figure 3a and Figure 3b is shown in Figure 4a and Figure 4b. The difference between the embodiments shown in Figures 3a/3b and Figures 4a/4b is that both the reservoir 4 and the detection cavity 5 in the embodiments shown in Figure 4a and Figure 4b are split up into a plurality of substantially identical reservoir/detection cavity sub-systems covering a substantial part of the inner side of said gas-impermeable disc 17. The functional principles of the embodiments shown in Figure 4a and Figure 4b correspond to those described in connection with the preceding embodiments and will hence not be described in detail here.

In the embodiments of the present invention according to Figures 3a, 3b, 4a and 4b

it is possible to provide the inner side of the disc 17 with a system of partially open channels where the openings are in contact with the surface 20 of the patient's skin or organ, and where the channels can be connected to a suitable vacuum source. Application of vacuum to the channels ensures a firm attachment of the disc 17 to the skin or organ of the patient.

Figure 5 shows the response of the sensor in volts as a function of time obtained in an experiment where water moves through a sand-filled tube simulating a bloodflow through tissue. The velocity of the water changed suddenly from 4.8 micrometers/second to the left of the arrow in the Figure to 24.8 micrometers/second immediately to the right of the arrow. A response time of approximately 0.5 - 1.0 minutes is possible, although the response time varies as a function of perfusion, and increases when the velocity through the tissue changes from a relatively high level to a relatively low level and vice versa.

Figure 6 shows a calibration curve obtained in the same experiment as in Figure 5, i.e. a curve of the signal from the detection device in Volts as a function of the velocity of water in mm/second.

Above, a number of different embodiments of the present invention have been shown and described, but it is understood that these embodiments only constitute examples of the general inventive idea as defined in the accompanying claims, and that other embodiments of the present invention might be conceivable by a person skilled in the art.

CLAIMS

1. Sensor for the measurement of tissue perfusion comprising a reservoir (4) for containing at least one fluid or gaseous tracer and being defined by a reservoir wall having a tracer-permeable reservoir wall portion, and a detection cavity (5) defined by a detection cavity wall having a tracer-permeable detection cavity wall portion, said tracer-permeable wall portions of the reservoir wall and the detection cavity wall, respectively, communicating with the surroundings, characterised in that the reservoir (4) and the detection cavity (5) are mutually interspaced, elongated cavities and that the tracer-permeable reservoir wall portion (3; 14') and the tracer-permeable detection cavity wall portions (3; 15') are elongated side wall portions.

2. Sensor according to claim 1, characterised in that the reservoir (4) and the detection cavity (5) are cylindrical and arranged in parallel.

3. Sensor according to claim 1 or 2, characterised in that the tracer-permeable wall portion (14') of the reservoir (4) and the tracer-permeable wall portion (15') of the detection cavity (5) are separate, mutually interspaced wall portions.

4. Sensor according to claim 3, characterised in that the reservoir (4) and the detection cavity (5) are separated by a tracer-impermeable barrier (19).

5. Sensor according to claim 3, characterised in that the reservoir (4) is defined by a tracer-permeable, tubular body (14) and that the detection cavity (5) is defined by a tracer-permeable, tubular body (15), and further that two bodies (14, 15) are interconnected by means of the tracer-impermeable barrier (19).

6. Sensor according to claim 1 or 2, characterised in that the tracer-permeable wall portion of the reservoir (4) and the tracer-permeable wall portion of the detection cavity (5) both are formed by a common tracer-permeable barrier (3) made from a tracer-permeable material, said tracer-permeable barrier (3) having a first longitudinally extending surface (18) being in contact with the surroundings, a second longitudinally extending surface (13) defining a portion of the detection cavity (5) and a third longitudinally extending surface (12) defining a portion of the tracer reservoir (4).

7. Sensor according to claim 6, characterised in that the tracer reservoir (4) is partly defined by a substantially U-shaped profile member (1), and that the detection cavity (5) is partly defined by a substantially U-shaped profile member (2) and further that the tracer-permeable barrier (3) sealingly engages the U-shaped profile members (1, 2) so as to close open sides (12, 13) thereof.

8. Sensor according to any of the claims 1 - 7, characterised in that the tracer-permeable reservoir wall portion (3; 14') and the tracer-permeable detection cavity wall portion (3; 15') extend substantially over the entire length of the sensor.

9. Sensor according to any of the claims 1-8, characterised in that the sensor is substantially symmetrical about a longitudinal plane (11).

10. Sensor according to any of the claims 1-9, characterised in that it comprises a series of reservoirs (4) and detection cavities (5) placed in side-by-side relationship.

SENSOR FOR MEASURING TISSUE PERFUSION

ABSTRACT OF THE INVENTION

The invention relates to a method and a sensor for measurement of tissue perfusion. The sensor is provided with a reservoir (4) for a fluid or gaseous tracer and a tracer-permeable barrier (3), a sub-surface of which is in contact with the surrounding tissue and another sub-surface of which is in contact with a detection cavity (5) which is connected to a suitable apparatus for the measurement of tracer concentration in the detection cavity. The concentration of the tracer in the detection cavity is a measure of perfusion in the surrounding tissue. According to another embodiment of the invention it is also possible to carry out measurements of perfusion in the surface layers of the skin or of an organ.

(It is suggested that Figure 1 be published with the Abstract).

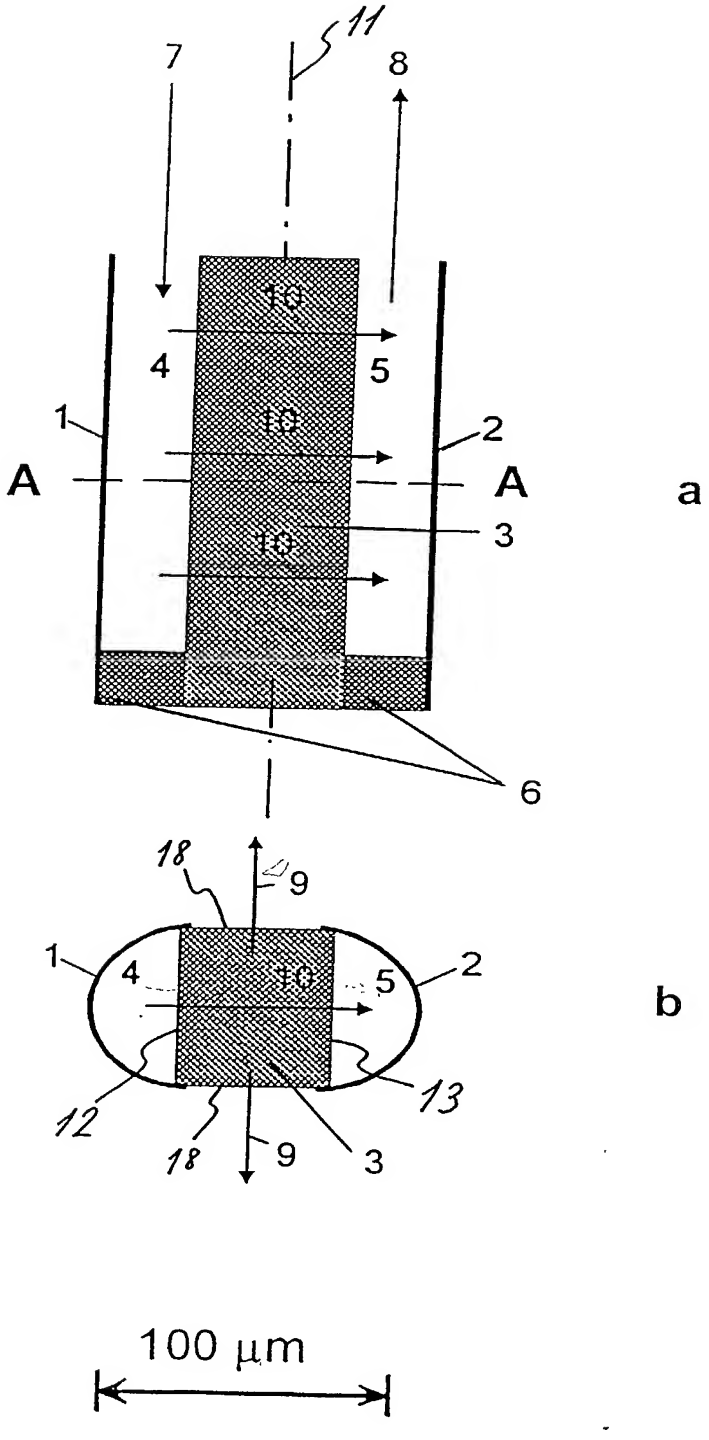

Fig. 1

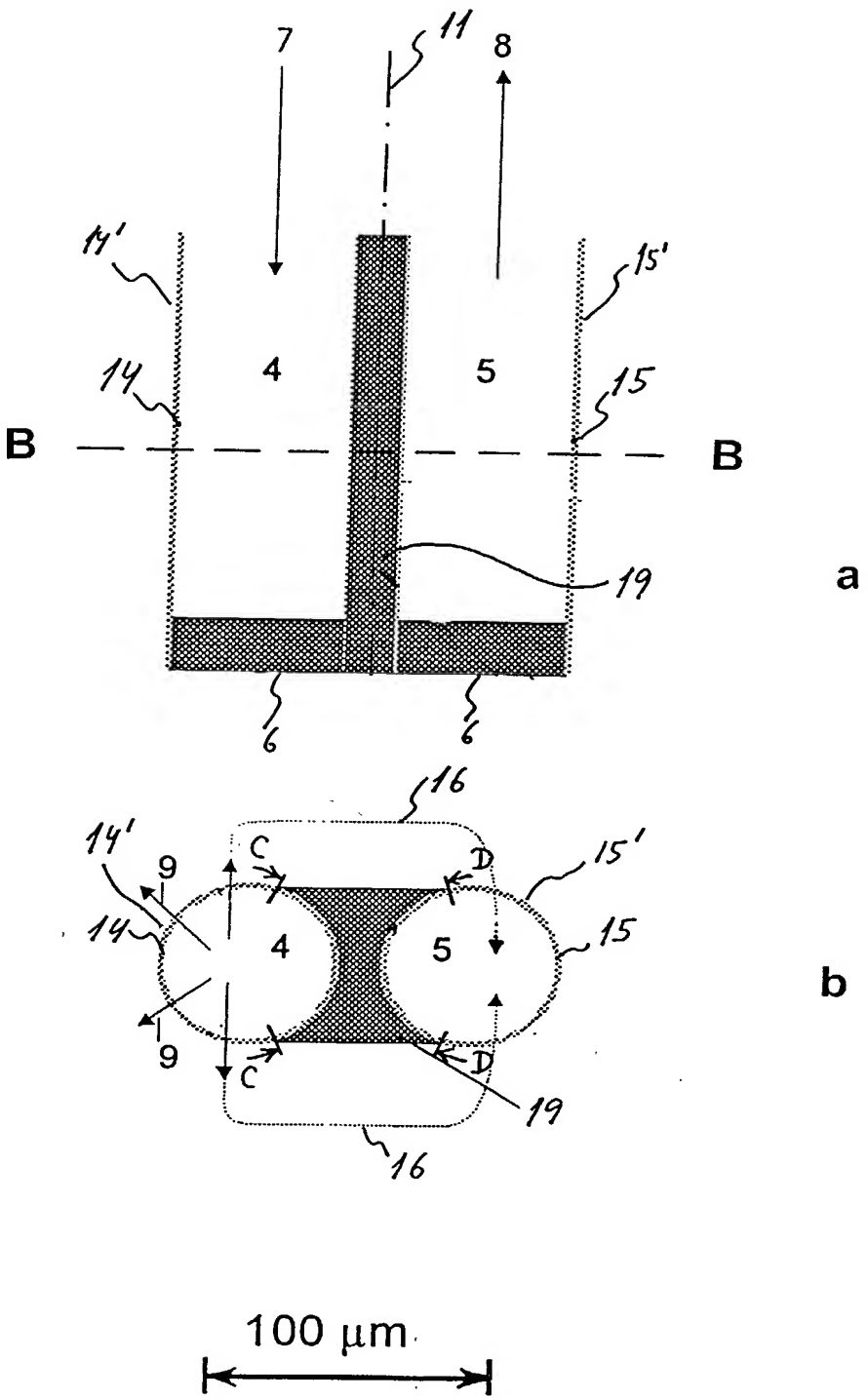

Fig. 2

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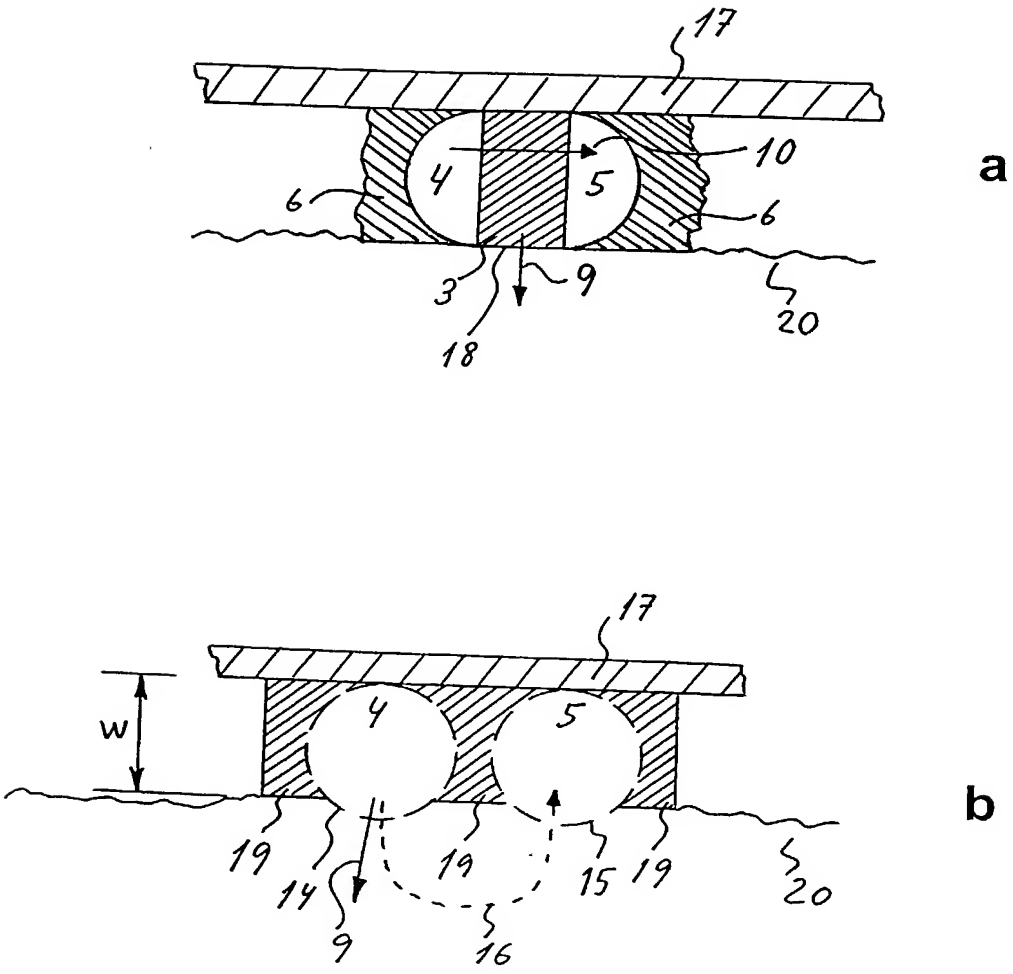
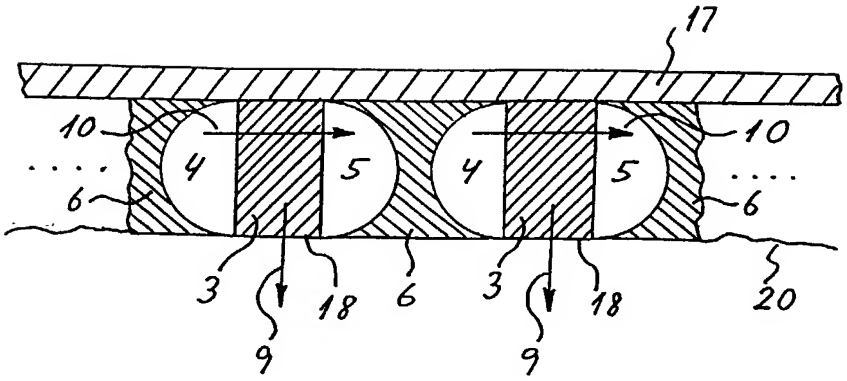


Fig. 3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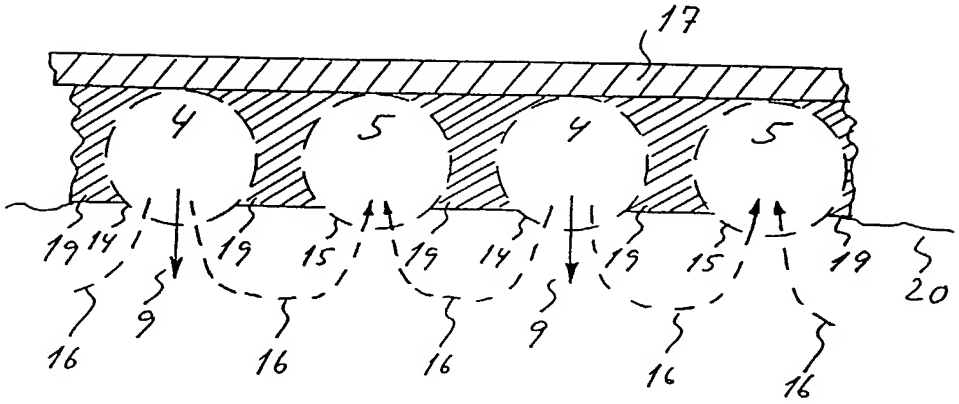
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16

b

Fig. 4

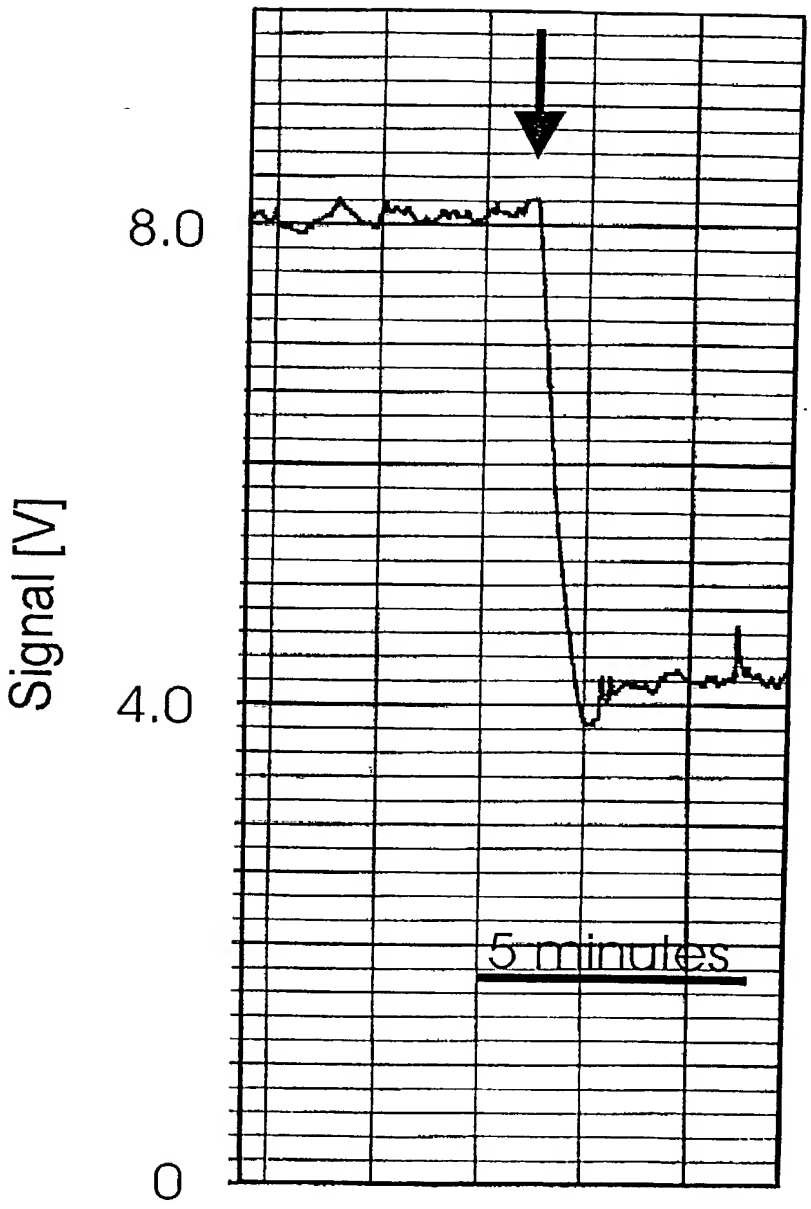

Fig. 5

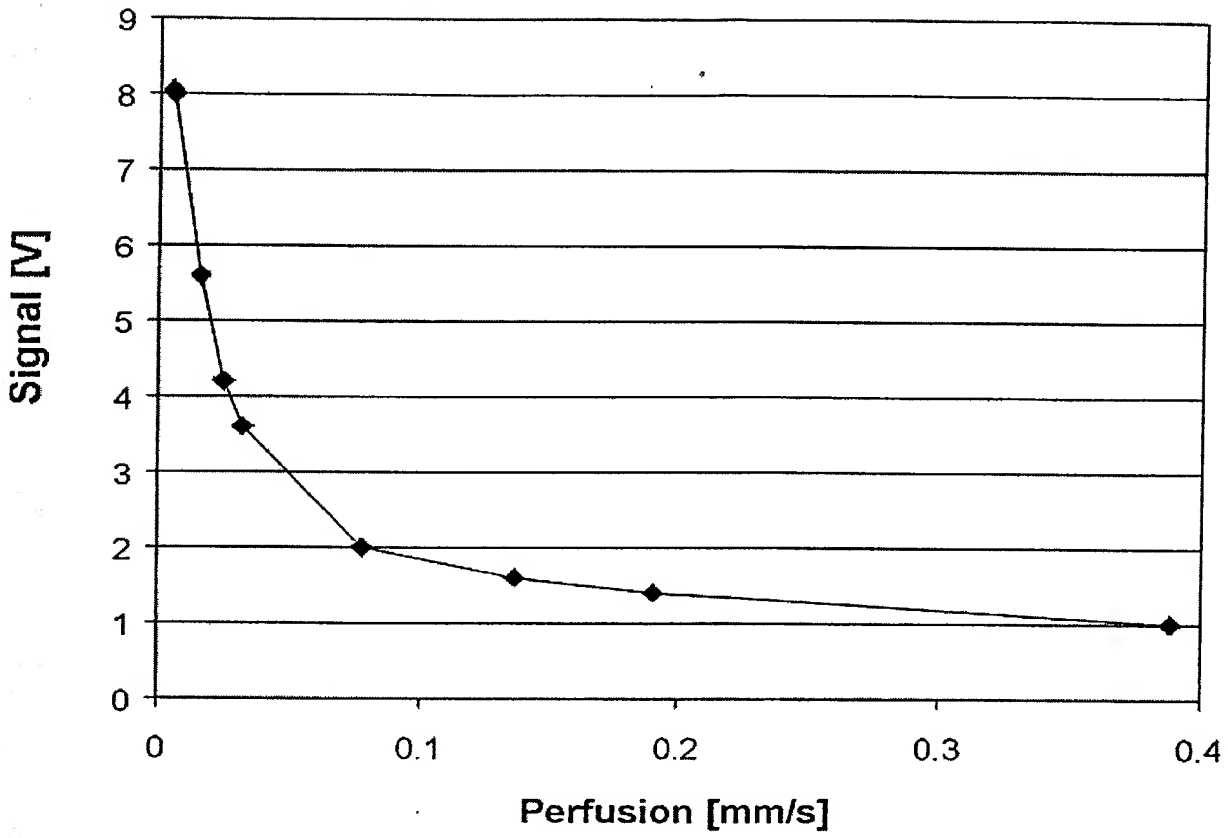

Fig. 6

#3

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **Sensor For Measuring Tissue Perfusion**, the specification of which:

__ is attached hereto.

_x_ was filed on March 20, 2002, as 10/088,582

Application Serial No. _____

and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)

			Priority Claimed	
Country	**Number**	**Date Filed**	**Yes**	**No**
Denmark	PCT/DK99/00522	04 Oct 1999	x	

I hereby claim the benefit under Title 35, United States Code Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

Application Serial No.	**Filing Date**	**Status**

And I hereby appoint William M. Lee, Jr., Registration No. 26,935; David C. Brezina, Registration No. 34,128; Thomas E. Smith, Registration No. 18,243; Dennis M. McWilliams, Registration No. 25,195; James R. Sweeney, Registration No. 18,721; Glenn W. Ohlson, Registration No. 28,455; Jeffrey R. Gray, Registration No. 33,391; Gerald S. Geren, Registration No. 24,528; Timothy J. Engling, Registration No. 39,970; Robert F. I. Conte, Registration No. 20,354; Howard B. Rockman, Registration No. 22,190; Peter J. Shakula, Registration No. 40,808; John W. Hayes, Registration No. 33,900; Mark A. Hagedorn, Registration No. 44,731; Mark J. Nahnsen, Registration No. 51,093; Gregory B. Beggs, Registration No. 19,286, to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith. It is requested that all communications be directed to Lee, Mann, Smith, McWilliams, Sweeney & Ohlson, P.O. Box 2786, Chicago, Illinois 60690-2786, telephone number (312) 368-1300.

16.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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